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Insertion of phosphoglycerine kinase (PGK)-neo 5' of Jlambda1 dramatically enhances VJlambda1 rearrangement.

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Gene-targeted mice were generated with a loxP-neomycin resistance gene (n cassette inserted upstream of the Jlambda1 region and replacement of the gly codon in the Clambda1 gene with a serine codon. This insertion dramatically increases Vlambda1-Jlambda1 recombination. Jlambda1 germline transcripti in pre-B cells and thymus cells are also greatly increased, apparently due to t housekeeping phosphoglycerine kinase (PGK) promoter driving the neo gene contrast, deletion of the neo gene causes a significant decrease in VJlambda1 recombination to levels below those in normal mice. This reduction is due to site left on the chromosome which reduces the Jlambda1 germline transcripti Thus, the correlation between germline transcription and variable (V), divers and joining (J) recombination is not just an all or none phenomenon. Rather, transcription efficiency is directly associated with the recombination efficien Furthermore, Jlambda1 and Vlambda1 germline transcription itself is not suf lead to VJ recombination in T cells or early pre-B cells. The findings may su in vivo: (a) locus and cell type-specific transactivators direct the immunoglol cell receptor loci, respectively, to a "recombination factory" in the nucleus, a transcription complexes deliver V(D)J recombinase to the recombination sig sequences.

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LEDGF regulation of alcohol and aldehyde dehydrogenases in l epithelial cells: stimulation of retinoic acid production and prot from ethanol toxicity.

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Retinoic acid (RA) is required for the normal growth and maintenance of ma types, including lens epithelial cells (LECs). Alcohol (ADH) and aldehyde (A dehydrogenases are implicated in cellular detoxification and conversion of vi to RA. Lens epithelium-derived growth factor (LEDGF) provides cellular pr against stress by transactivating stress-associated genes. Here we show evide LEDGF binds and transactivates heat shock (nGAAn) and stress response (A/TGGGGA/T) elements in the promoters of ADH1, ADH4, and retinaldeh (RALDH2) genes. Electrophoretic mobility and supershift assays disclosed s binding of LEDGF to nGAAn and A/TGGGGA/T elements in these gene pr Transfection experiments in LECs with promoters linked to a chloramphenic acetyltransferase (CAT) reporter gene along with LEDGF cDNA revealed hi CAT activity. RT-PCR results confirmed that LECs overexpressing LEDGF contained increased levels of ADH1, ADH4, and RALDH2 mRNA. Notably, displayed higher LEDGF mRNA and protein expression during ethanol stres overexpressing LEDGF typically exhibited elevated RA levels and survived during ethanol stress. The present findings indicate that LEDGF is one of the transcriptional activators of these genes that facilitates cellular protection aga ethanol stress and plays a role in RA production.

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